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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,621	12/11/2003	Atul Varadhachary	HO-P02705US2	8531

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EXAMINER	
KAM, CHIH MIN	
ART UNIT	**PAPER NUMBER**
1656	

DATE MAILED: 12/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/733,621	VARADHACHARY ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-22 and 35-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-22 and 35-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The Request for Continued Examination (RCE) filed on November 10, 2005 under 37 CFR 1.114 is acknowledged. An action on the RCE follows.

Status of the Claims

2. Claims 1, 3-22 and 35-37 are pending.

Applicants' amendment filed on September 12, 2005 is acknowledged. Applicants' response has been fully considered. Claims 1 and 35 have been amended. Thus, claims 1, 3-22 and 35-37 are examined.

Withdrawn Claim Rejections - 35 USC § 102

3. The previous rejection of claims 1, 3-7 and 11-22 under 35 U.S.C. 102(e) as anticipated by Kruzel *et al.* (US 2003/0096736, filed May 7, 2002), is withdrawn in view of applicant's amendment to the claim, and applicant's response at pages 5-6 of the amendment filed September 12, 2005.

Withdrawn Claim Rejections - 35 USC § 103(a)

4. The previous rejection of claims 35-36 under 35 U.S.C. 103(a) as being unpatentable over Olmarker *et al.* (WO 02/080891) in view of Hanson *et al.* (WO 00/01730), is withdrawn in view of applicant's amendment to the claim, and applicant's response at page 6 of the amendment filed September 12, 2005.

New Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 6 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 6 is indefinite because of the use of the term "wherein said lactoferrin is human or bovine". The cited term renders the claim indefinite, it is not clear how the lactoferrin can be human or bovine.

7. Claim 21 is indefinite as to what cytokines having the production or activity enhanced by lactoferrin, since lactoferrin also reduces the production or activity of pro-inflammatory cytokines which should be differentiated from the cytokines having the production or activity being enhanced by lactoferrin.

New Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the

reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

8. Claims 1, 3-6, 13 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Mita *et al.* (U.S. Patent 5,561,109, published on October 1, 1996).

Mita *et al.* teach lactoferrin, lactoperoxidase or a combination thereof, either alone or in admixture with at least one excipient can be used for treating corneal injury caused by ulceration, inflammation or ophthalmological surgery, where lactoferrin and lactoperoxidase significantly accelerate the regeneration of corneal keratocytes in the in vivo test (column 1, lines 35-67; column 3, lines 24-column 4, line 3), and where the lactoferrin can be obtained from milk of human or bovine (claims 4-6) and can be administered orally or parenterally, preferably as eye drops, and where 0.5 wt % eye drops of lactoferrin dissolved in physiological saline was instilled 10 times per day at one hour intervals (0.5 g/100 ml x 0.05 ml (per drop) x 10 = 2.5 mg; claims 13 and 18). Although the reference does not specifically indicate administration of lactoferrin would treat a subject suffering from pain due to surgery, the reference teaches the same method step (i.e., administering an effective amount of lactoferrin in the animal corneal burn model) as the claimed method, thus it would be expected that administration of lactoferrin would have provided an improvement in the treatment of pain for a subject undergoing corneal injury caused by ophthalmological surgery (claims 1 and 3).

9. Claims 1, 3-6, 11, 15, 16 and 18-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Ando *et al.* (US 2004/0018190, filed on November 22, 2001).

Ando *et al.* teach lactoferrin tablets were produced by mixing 50 mg of lactoferrin powder with lactose, cellulose and carboxymethylcellulose calcium salt in a dry state (Example

7), and enteric lactoferrin tablets were administered to a patient suffering from a recurrence of gastric cancer after a surgical operation and retention of cancerous abdominal fluid (paragraph [0056]). In this case, the abdominal fluid was drawn several times a week to relive pain, after orally taking enteric lactoferrin tablets (lactoferrin dose: 0.45 g per day) for a week, the abdominal fluid was completely absorbed and eliminated (claims 1, 3, 4, 11, 15, 18 ad 19). The reference also indicates lactoferrin can be obtained from bovine milk (paragraphs [0011], [0017]; claim 5 and 6), and enteric lactoferrin tablets can deliver the lactoferrin to the lower digestive tract (the duodenum and small intestine; paragraph [0021]; claim 16). Although the reference does not specifically indicate administration of lactoferrin reduces the production or activity of pro-inflammatory cytokines or enhances the production or activity of some cytokines, since the reference teaches the same method steps, it would be expected that administration of lactoferrin would have produced these effects (claims 20-22).

New Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1, 3-8, 11-13, 15, 20-22 and 35 under 35 U.S.C. 103(a) as being obvious over Wu *et al.* (U. S. Patent 5,712,247, published January 27, 1998).

Wu *et al.* teach lactoferrin and its N-terminal fragment (residues 1 to 61) may be used to neutralize and regulate the activity of heparin in the patients undergoing cardiovascular surgery

and other surgical procedures by modulating heparin-serpin and heparin thrombin interactions, where lactoferrin can be purified from human milk or recombinantly produced (column 4, lines 21-61; claims 1, 5-8 and 35). The reference also indicates lactoferrin can be mixed with suitable carriers to form a pharmaceutical formulation for oral, topical, or intestinal or parenteral administration or sustained release at doses to treat or ameliorate a variety of diseases related to the activity of heparin (column 5, line 5-column 7, line 22; claims 4, 11-13, 15). Although Wu *et al.* do not specifically teach using lactoferrin to treat a subject suffering from pain, the reference suggests the use of an effective amount of lactoferrin in the treatment of patients undergoing cardiovascular surgery and other surgical procedures by modulating heparin-serpin and heparin thrombin interactions, thus, it would be obvious that the administration of lactoferrin would inherently provide an improvement in the pain associated with cardiovascular surgery and other surgical procedures (claims 1 and 3). Although Wu *et al.* do not specifically indicate lactoferrin reduces the production or activity of pro-inflammatory cytokines (e.g., TNF-α), or enhances the production or activity of certain cytokines (e.g., IL-18), the reference teaches the same method step (the administration of lactoferrin) as the claimed invention, where the lactoferrin would be expected to produce these effects (claims 20-22).

11. Claims 1, 3-7 and 11-22 under 35 U.S.C. 103(a) as being obvious over Kruzel *et al.* (US 2003/0096736, filed May 7, 2002).

Kruzel *et al.* teach lactoferrin (LF) tablets containing 95.45 parts dextrose, 2.97 parts bovine LF, and 0.53 parts calcium stearate (a known antacid) or a capsule (25 mg) is made (paragraph [0040]) and can be administered to treat autoimmune conditions such as cancer, where lactoferrin may be human lactoferrin, either natural or recombinant, or bovine milk

lactoferrin (paragraphs [0022], [0033], [0034]; claims 1, 4-7, 11, 14). The reference also indicates lactoferrin can be administered enteraly (claims 15-17), preferably orally, or parenterally, preferably intravenously (claim 12), in the form of injectable solution, or, as a liposomal formulation such as transdermal patches (claim 13), and a single or twice daily dose of 0.01 mg to 20 mg of lactoferrin per kg of body weight is administered (paragraph [0038]; corresponding to 0.6 mg to 1.2 g per day assuming single dose/day and body weight of 60 kg; claims 18 and 19). Although Kruzel *et al.* do not specifically teach using lactoferrin to treat a subject suffering from pain, the reference suggests the use of the same effective amount of lactoferrin (e.g., 0.6 mg to 1.2 g per day, which is in the range of 1 ng to 100g per day used in the claimed method, see paragraph [0073] of US 2004/0151784 (10/733,621)) in the treatment of cancer patients, thus, it would be obvious that the administration of lactoferrin would inherently provide an improvement in the pain associated with cancer (claims 1 and 3). Although Kruzel *et al.* do not specifically indicate lactoferrin reduces the production or activity of pro-inflammatory cytokines (e.g., TNF-α), or enhances the production or activity of certain cytokines (e.g., IL-18), the reference teaches the same method step (the administration of lactoferrin) as the claimed invention, where the lactoferrin would be expected to produce these effects (claims 20-22).

Claim Rejections-Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1, 3-22 and 35-37 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 and 12 of copending Application No. 10/862,213 (now available as US-PGPub 2005/0019342). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 3-22 and 35-37 in the instant application disclose a method of treating a subject suffering from pain comprising administering to the subject an effective amount of a lactoferrin composition to provide an improvement in pain in the subject, wherein the pain is associated with cancers or surgery; or a method of treating a subject suffering from pain comprising administering to the subject an effective amount of a lactoferrin composition consisting essentially of N-terminal variant to provide an improvement in pain in the subject, where the pain is associated with cancers, disorders of the central nervous system or surgery. This is an obvious variation in view of claims 1-8 and 12 in the copending application which disclose a method of treating cancer comprising administering to a subject a cancer immunotherapy and an adjuvant, wherein said adjuvant is a lactoferrin composition that is administered in an amount sufficient to provide improvement in the cancer in the patient; and the specification discloses the lactoferrin composition comprises lactoferrin or an N-terminal lactoferrin variant (paragraph [0009]), where the N-terminal lactoferrin variant mediates the same biological activity as full-length lactoferrin, e.g., stimulating the production of various cytokines (e.g., IL-18) and inhibits the production of various pro-inflammatory cytokines (e.g., TNF-α), and improves parameters

which promote or enhance the well-being of subject with respect to the medical treatment of cancer, e.g., a decrease in pain to the subject that can be attributed to the subject's condition (paragraphs [0043], [0059]); and the lactoferrin composition can be administered orally, parentally or topically, for oral administration, an antacid can be administered in conjunction with the lactoferrin composition (paragraph [0012]). Both the claims of instant application and the claims of the copending application are directed to a method of treating a patient suffering from cancer comprising administering an effective amount of a lactoferrin composition to provide improvement in the cancer of the patient such as the pain associated with cancer. Thus, claims 1, 3-22 and 35-37 in present application and claims 1-8 and 12 in the copending application are obvious variations of a method of treating a patient suffering from cancer comprising administering an effective amount of a lactoferrin composition to provide improvement in the cancer of the patient such as the pain associated with cancer.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to the Arguments

Applicants indicate since the co-pending application may never actually issue, or, the claims as originally filed may be amended during the course of prosecution of the co-pending application, and the rejection remains "provisional" until co-pending application issues. As such, Applicants are not required to address the merits of the provisional double-patenting rejections until such time as the co-pending applications actually issue (pages 6-7 of the response).

Applicants' response has been considered, however, the argument is not found persuasive, and the rejection is maintained.

13. Claims 1, 3-7, 11-13, 15-17, 20-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8, 13-17, 24, 28, 42-50 and 73-79 of copending Application No. 10/434,769 (now available as US-PGPub 2004/0009895). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 3-7, 11-13, 15-17, 20-22 in the instant application disclose a method of treating a subject suffering from pain comprising administering to the subject an effective amount of a lactoferrin composition to provide an improvement in pain in the subject, wherein the pain is associated with cancers or surgery. This is an obvious variation in view of claims 1-8, 13-17, 24, 28, 42-50 and 73-79 in the copending application which disclose a method of treating hyperproliferative disease such as cancer comprising administering to a subject a human lactoferrin in an amount sufficient to provide an improvement in the hyperproliferative disease. Both the claims of instant application and the claims of the copending application are directed to a method of treating a patient suffering from cancer comprising administering an effective amount of a lactoferrin composition to provide improvement in the condition. Thus, claims 1, 3-7, 11-13, 15-17, 20-22 in present application and claims 1-8, 13-17, 24, 28, 42-50 and 73-79 in the copending application are obvious variations of a method of treating a patient suffering from cancer comprising administering an effective amount of a lactoferrin composition to provide improvement in the condition of the patient such as the pain associated with cancer.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

14. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Patent Examiner

CHIH-MIN KAM
PATENT EXAMINER

CMK
December 21, 2005